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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/710,760	11/10/00	ROYER J	5563.210-US

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HM12/0328

EXAMINER	
GANSHERDFF, I	
ART UNIT	**PAPER NUMBER**
1636	4

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/710,760	Applicant(s) ROYER ET AL.	
	Examiner Lisa Gansheroff	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *70-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *72-78* is/are rejected.

7)☒ Claim(s) *75* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 November 2000* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *Attachment pages* .

DETAILED ACTION

Pending claims: 70-78.

Response to: Preliminary Amendment filed 10 November 2000.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 70-76 been renumbered 72-78.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 70 and 71, drawn to a mutant cell and to a method for producing a polypeptide comprising cultivating the mutant cell, classified in class 435, subclasses 69.1 and 254.7.

II. Claims 72-78, drawn to an isolated trichodiene synthase, classified in class 530, subclass 371.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are

not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are biologically, chemically, and functionally different. A mutant cell is entirely different structurally and chemically from an isolated trichodiene synthase, as trichodiene synthase is just one polypeptide. A mutant cell is biologically and functionally different from a trichodiene synthase, as a mutant cell performs many different molecular reactions, none of which need correspond to the activity of a trichodiene synthase. A method for producing a polypeptide comprising cultivating a mutant cell is distinct from a trichodiene synthase, since the polypeptide produced can be any polypeptide and need not be trichodiene synthase, an isolated trichodiene synthase is not required for a mutant cell to produce a polypeptide, and a trichodiene synthase can be produced in vitro without cultivating any cells, such as with a machine that synthesizes polypeptides from amino acids. Thus, these different inventions are capable of supporting separate patents.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

During a telephone conversation with Robert Starnes on 21 February, 2001, a provisional election was made with traverse to prosecute the invention of Group II, claims 72-78. Affirmation of this election must be made by applicant in replying to this Office action. Claims 70 and 71 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the

inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Drawings

The drawings are objected to because of the following. Parts of the top lines of Figs. 2A-2E are obscured by the hole-punches in the tops of the pages required for insertion of the application into the file jacket. Correction is required.

Specification

The disclosure is objected to because of the following informalities: On nearly all of the pages, words in the top one or two lines are obscured by the hole-punches put in the pages for inserting them into the file jacket.

Appropriate correction is required.

Priority

If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title,

preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Sequence compliance

Acknowledgement is made of the receipt of a paper copy and computer readable form of the sequence listing and of the Applicant's statement that these are the same. As requested by Applicants, the computer readable form from the parent case 09/316,080 has been used as the computer readable form for the instant case. The sequence listing from the computer readable form has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 72-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 72 recites "an allelic variant of (a) or (b)". Part (a) recites a trichodiene synthase

with an amino acid sequence at least 97% identical with SEQ ID NO:2, and part (b) recites a variant of trichodiene synthase comprising a substitution, deletion, and/or insertion of one or more amino acids. The term "allelic variant" is defined in the specification on page 22 as "any or two or more alternative forms of a gene occupying the same chromosomal locus. Allelic variation arises naturally through mutation." Thus, it is not clear what is meant by an "allelic variant" of a sequence that is not naturally-occurring, such as many sequences encompassed by parts (a) and (b), as contrasted with an "allelic variant" of a sequence that is naturally-occurring at a given chromosomal locus, such as SEQ ID NO:2 itself.

Claim 72 recites a "variant of the trichodiene synthase having an amino acid sequence of SEQ ID NO:2 comprising a substitution, deletion, and/or insertion of one or more amino acids". This phrase renders the metes and bounds of the claim indefinite, because it not known how many substitutions, deletions, and/or insertions would be permitted for a "variant" to remain within the bounds of the claim. For example, there are no functional limitations in part (b).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 77 and 78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that strain "ATCC 20334" is required to practice the claimed invention of claim 77. Thus, this must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the strain. While it is clear that the strain has been deposited at the ATCC, it is not clear that it was deposited by the instant inventors. If it was not, then it is not clear, for example, that it would be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer, or that access to the material will be available during the pendency of the patent application. Please see the deposit information below.

It is apparent that strain "NRRL B-30029" is required to practice the claimed invention of claim 78. Thus, this must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the strain. While the specification states that Applicants deposited the strain, it is not clear that all restrictions have been removed. Please see the deposit information below, especially the paragraph following section 7.

A suggestion for deposit of biological materials is provided:

A declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection

based on a lack of availability of biological material. See 37 CFR 1.801 through 1.809. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent.

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122.

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977), that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent, and that the deposited material will be maintained for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

Claims 72-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 72, 74, and 76 are drawn to a genus of trichodiene synthases which can have the amino acid sequence of SEQ ID NO:2, which can be fragments with trichodiene synthase activity, or which can be variants or allelic variants of SEQ ID NO:2. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Applicants have not disclosed any "fragment" of SEQ ID NO:2 which has trichodiene synthase activity. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, and/or insertions that may be made to SEQ ID NO:2, and these variants need not retain full or even partial activity. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification also does not disclose any "allelic" variants of SEQ ID NO:2; the specification on page 22 states that "allelic" variants are on the same chromosomal locus, and only one *Fusarium venenatum* trichodiene synthase is disclosed. Further, regarding variants, while techniques for making changes to an amino acid sequence are known in the art, the specification and claims do not provide guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class (such as other trichodiene synthases or other amino acid sequences

without trichodiene synthase activity) are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is needed. A correlation of structural features with function is not disclosed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant in structure and in function, SEQ ID NO:2 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 72, recites an isolated trichodiene synthase obtained from a *Fusarium venenatum* strain, and part (b) is drawn to a variant of the trichodiene synthase having an amino acid sequence of SEQ ID NO:2 comprising a substitution, deletion, and/or insertion of one or more amino acids. Thus, claim 72 and the dependent claims encompass a product-by-process embodiment; that is, a "variant" trichodiene synthase could be obtained by introducing a

substitution, deletion, or insertion into SEQ ID NO:2 from *Fusarium venenatum*, or the variant trichodiene synthase of part (b) could also be isolated from a different organism. See MPEP 2113, which states the following: "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. ... The patentability of a product does not depend on its method of production."

Claims 72, 73, and 76 are rejected under 35 U.S.C. 102(b) as anticipated by Hohn et al. (1992. Molecular Plant-Microbe Interactions 5:249-256, on Applicant's IDS).

Hohn et al. teach a trichodiene synthase from *Giberella pulicaris*. The amino acid sequence is shown in Fig. 2. A sequence search shows a 98.8% query match and a 98.2% best local similarity with SEQ ID NO:2. See Result 1 on the attached search print-out titled "us-09316-080-2.rsp". Thus, the trichodiene synthase of Hohn et al. is a variant of SEQ ID NO:2 comprising a substitution, deletion, and/or insertion of one or more amino acids.

Claims 72 and 76 are rejected under 35 U.S.C. 102(b) as anticipated by Hohn et al. (1989. Gene 79:131-138, on Applicant's IDS).

Hohn et al. teach a trichodiene synthase from *Fusarium sporotrichioides*. See Figure 2. A sequence search shows a 94.7% query match of the sequence of Hohn et al. with SEQ ID NO:2. See Result 3 on the attached search print-out titled "us-09316-080-2.rsp". Thus, the trichodiene synthase of Hohn et al. is a variant of SEQ ID NO:2 comprising a substitution, deletion, and/or insertion of one or more amino acids.

Claims 72 and 76 are rejected under 35 U.S.C. 102(b) as anticipated by Proctor et al. (1995. Molecular Plant-Microbe Interactions 4:593-601, on Applicant's IDS).

Proctor et al. teach a trichodiene synthase from *Giberella zeae*. The amino acid sequence is shown in Fig. 2. A sequence search shows a 91.2% query match with SEQ ID NO:2. See Result 4 on the attached search print-out titled "us-09316-080-2.rsp". Thus, the trichodiene synthase of Proctor et al. is a variant of SEQ ID NO:2 comprising a substitution, deletion, and/or insertion of one or more amino acids.

Claims 72 and 76 are rejected under 35 U.S.C. 102(a) as anticipated by Trapp et al. (1998. Molecular and General Genetics 257:421-432).

Trapp et al. teach a trichodiene synthase from *Myrothecium roridum*. The amino acid sequence is shown in Fig. 3. A sequence search shows a 74.4% query match with SEQ ID NO:2. See Result 6 on the attached search print-out titled "us-09316-080-2.rsp". Thus, the trichodiene synthase of Trapp et al. is a variant of SEQ ID NO:2 comprising a substitution, deletion, and/or insertion of one or more amino acids.

Allowable Subject Matter

Claim 75 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Gansheroff whose telephone number is (703) 605-1203. The examiner can normally be reached 9 AM - 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached at (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242 for regular communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Dianiece Jacobs whose telephone number is (703) 305-3388 or to the receptionist whose telephone number is (703) 308-0196.

LG
March 21, 2001